ESTABLISHING A NOVEL CELL THERAPY PLATFORM: SYNTHETIC BIOLOGY AND BIOPROCESS CONSIDERATIONS FOR RATIONAL THERAPEUTIC DEVELOPMENT

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Cell therapies offer exciting, novel strategies for treating acute, chronic, and incurable diseases. This technology represents a “eureka moment,” according to the former FDA head, Scott Gottlieb. This field has undergone several generations of development, from stem cell transplantation, to dendritic cell modification, and developing most recently into autologous CAR-T therapies that have been highly effective against some blood cancers. However, these recent autologous therapies have been limited by daunting costs, highly variable process outcomes, a lack of reliable assays, and supply chains that are both immature and risky. Call this Cell Therapy 1.0. Allogeneic therapies, either from primary donors or induced pluripotent lines, or Cell Therapy 2.0, are being currently developed. As these are nucleated cells with the potential for significant expansion in vivo, they still carry substantial safety concerns. Rubius Therapeutics is leapfrogging the allogeneic adoptive transfer approaches by developing Red Cell Therapeutics™, in which therapeutic proteins are expressed in or on genetically engineered, enucleated red blood cells. This versatile, innovative 3.0 platform enables us to efficiently target immune-oncology, inborn metabolic disorders, and autoimmune indications. It also makes cell therapy more akin to a routine monoclonal antibody business model with greater scale, flexibility, reliability, and cost competitiveness relative to current autologous and allogeneic technologies. However, the traditional process metrics used in manufacturing monoclonal antibodies must be adjusted to account for the unique considerations of red cell manufacture. Rubius monitors a variety of phenotypical and product-specific biomarkers that track the progression of cells through erythroid differentiation in conjunction with seed train steps in the process. Methods to understand which attributes are predictive of process outcome and final product quality are at the forefront of Rubius’ analytical strategy. By understanding allogeneic cell manufacturing – specific process development challenges and developing analytical methods capable of reliably predicting process performance and product quality, Rubius expects to develop the next generation of cellular therapies that are cost effective, consistent, and efficacious against incurable diseases.